

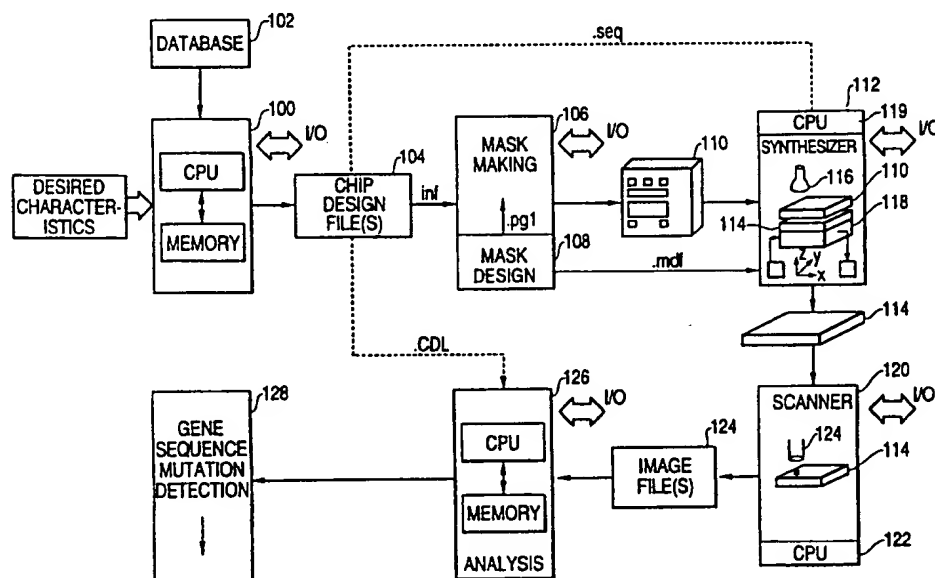


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(54) Title: ARRAY FABRICATION METHODS



(57) Abstract

There is provided modified methods and apparatus for the preparation of arrays of material wherein each array includes a preselected collection of polymers, small molecules or inorganic materials associated with a surface of substrate. The methods provide for modifications to general apparatus, flow cell geometries and solutions used in array fabrication. In one embodiment a method of removing static charge during the fabrication of an array is described. The method of static charge removal may include, but is not limited to, use of an ionizing fan or ion bars. In particular, equipment for removing static charges is placed at each entry and exit point in the flow cell. In another embodiment optimized flow cell geometries are provided. In another embodiment the introduction of phosphoramidite during array fabrication is provided. In another embodiment a deprotection solution comprising alkylamine is provided.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/02515

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 B01J19/00 C07H21/00 C07B61/00		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) IPC 6 B01J C07B		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 874 916 A (WILLIAM R. LIVESAY & MALCOLM E. WING) 1 April 1975 (1975-04-01) abstract column 1, line 6 - line 11 column 2, line 37 - line 47 column 6, line 51 - line 58 column 7, line 64 - column 8, line 30 figures	1,2,5,13
A	---	42,44
X	US 5 167 326 A (ROBERT H. MURPHY) 1 December 1992 (1992-12-01) abstract column 1, line 39 - line 46 column 3, line 27 - line 30 column 7, line 38 - line 64 ---	1
-/-		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.		
<input checked="" type="checkbox"/> Patent family members are listed in annex.		
* Special categories of cited documents:		
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Date of the actual completion of the international search <div style="text-align: center; font-size: 1.2em;">14 June 1999</div>		Date of mailing of the international search report <div style="text-align: center; font-size: 1.2em;">24. 09. 99</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer <div style="text-align: center; font-size: 1.2em;">STEVNSBORG, N</div>

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 99/02515

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
13	A US 4 677 520 A (JAMES PRICE) 30 June 1987 (1987-06-30) abstract	6,9-12, 42,43,45
5	A US 5 679 773 A (CHRISTOPHER P. HOLMES) 21 October 1997 (1997-10-21) abstract column 10, line 46 - line 63	1-4,6-8
1	A EP 0 695 941 A (AFFYMAX TECHNOLOGIES N.V.) 7 February 1996 (1996-02-07) abstract	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 99/02515

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-13, 42-45, 50-52

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 99/02515

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-13, 42-45, 50-52

Independent claim 1, and its dependent claims 2-12, and 50-52 relating to a method of fabricating arrays comprising the fabrication of materials on a surface of a substrate to form an array of materials and removing static charge during the fabrication step.

Independent claim 13, and its dependent claims 42-45 relating to a method of fabricating arrays comprising the manipulation of static charge on a reactor and fabricating materials using said reactor.

2. Claims: 14-22

Independent claim 14 and its dependent claims 15-22 relating to a method of removing protective groups from nucleotides comprising the deprotection of the nucleotides with an alkylamine diluted in H₂O.

3. Claims: 23-34, 39-41, 46-49, 53-55

Independent claim 23 and its dependent claims 24-34 and 53-55 relating to a method of fabricating arrays comprising photolysis on a substrate with functional groups on its surface, where the photolysis takes place in a flow cell characterised by the dimensions thereof.

Independent claim 39 and its dependent claims 40-41 and 46-49 relating to a method of fabricating arrays comprising photolysis on a substrate with functional groups on its surface, and performing a chemical reaction inside a flow cell, characterised by the manufacturing of the flow cell.

4. Claims: 35-38

Independent claim 35 and its dependent claims 36-38 relating to a method of fabricating arrays comprising photolysis on a substrate with functional groups on its surface and performing a chemical reaction inside a flow cell, where the chemical reaction comprises the addition of a 3'-O-activated phosphoramidite nucleoside photoprotected at the 5'-hydroxyl.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 99/02515

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3874916 A	01-04-1975	NONE	
US 5167326 A	01-12-1992	US 5012924 A US 5109981 A	07-05-1991 05-05-1992
US 4677520 A	30-06-1987	EP 0236484 A JP 63500975 T WO 8701899 A	16-09-1987 07-04-1988 26-03-1987
US 5679773 A	21-10-1997	AU 689924 B AU 2948395 A CA 2193228 A EP 0776330 A JP 10507160 T US 5917016 A WO 9600378 A US 5739386 A	09-04-1998 19-01-1996 04-01-1996 04-06-1997 14-07-1998 29-06-1999 04-01-1996 14-04-1998
EP 695941 A	07-02-1996	AU 2943695 A EP 0764214 A JP 8166387 A JP 10505410 T WO 9533846 A	04-01-1996 26-03-1997 25-06-1996 26-05-1998 14-12-1995